what was covered by the claims in the original form. Support for these amendments are found throughout the specification and the originally filed claims.

More particularly, the claims have been amended to delete the term "anchoring" sequence and substitute therefor "locking" sequence. The term anchoring and locking sequence sometimes are used interchangeably in the specification. See *e.g.*, page 9, line 25-27, and page 19, lines 24-26. As indicated at page 19, an anchoring or locking sequence is a sequence that confers stable secondary structure to a localized portion of the sequence. Thus, a locking sequence is an anchoring sequence which forms a stable secondary structure. Examples include but are not limited to triplex formation (see *e.g.*, Figure 2c); quadruplex-formation (see *e.g.*, Figure 2d); and triplex formation with a secondary probe (see *e.g.*, Figure 2e).

The description of FIG. 2 has been amended pursuant to the Examiner's request to provide a legend for the filled-in squares versus the blank squares in the figure. Support for this amendment is found in Provisional Patent Application No. 60/130,345 from which the present application claims priority.

In addition, Applicants have amended claims 1, 22, 39, 60, 108 and 112 by substituting "containing/ contain" with "comprising/comprise."

No new matter is presented by these amendments, and entry thereof into the instant application is respectfully requested. A "Version with Markings to Show Changes Made" is attached hereto to show the amendments, and an "Appendix of Pending Claims", providing all the claims following entry of the present amendment, is also attached hereto for the Examiner's convenience.

Objection to the Specification

The Examiner has objected to the specification indicating that "Figure 2 lacked a clear indication of the claimed homology clamp and anchoring sequence." Applicants have amended the brief description for FIG. 2, support for which is found in the U.S. Provisional Patent Application from which the instant application claims priority. In making this amendment, Applicants do not concede or admit that "homology clamp" or "locking sequence" as used in the claims is limited to that depicted in or described in reference to

FIG. 2, as could possibly be interpreted by the Examiner's phrasing of the objection and Applicant's amendment to address the same.

Compliance With 37 CFR §1.821

The present Amendment complies with the requirements for patent applications containing nucleotide sequence and/or amino acid sequence disclosures in adherence with rules 37 C.F.R. § 1.821-1.825. This amendment is accompanied by a floppy disc containing the above named sequence, SEQUENCE ID NUMBERS 1-17 in computer readable form, and a paper copy of the sequence information. The computer readable sequence listing was prepared through use of the software program "PatentIn" provided by the PTO. The information contained in the computer readable disc is identical to that of the paper copy. This amendment contains no new matter. Applicant submits that this amendment, the accompanying computer readable sequence listing, and the paper copy thereof serve to place this application in a condition of adherence to the rules 37 C.F.R. § 1.821-1.825.

Claim Objections

The Examiner objected to Claim 43 as "polynucleotides" was improperly placed in the plural rather than the singular. Claim 43 has been amended accordingly to address this objection.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 10, 14, 18-21, 31, 33-42, 52 and 54-64 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite.

The Examiner argues that the recitation of "wherein at one of said targeting polynucleotides comprises protein nucleic acid" in claims 10, 31 and 52 is vague and indefinite. Applicants have amended claims 10, 31 and 52 to recite "peptide nucleic acid", support for which is found in the specification at (pg:ln) 13:17-31, where the term is defined clearly to mean DNA analogs with a peptide-like backbone.

The Examiner indicated that claims 14, 18, 33, 35, 36, 39, 54, 57 and 60 contain recitations that lack antecedent basis. Applicants have amended these claims to rectify

antecedent basis problems, and respectfully submit that the amended claims 14, 18, 33, 35, 36, 39, 54, 57 and 60 now have proper antecedent basis.

The Examiner argues that the recitation "purification moieties" in Claims 21, 42 and 63 is vague and indefinite. Applicants have amended the claims to recite "purification tag moieties" as suggested by the Examiner.

The Examiner argues that the recitation "containing" in Claim 64 is not legally defined as open or closed transitional language. Applicants have amended the claim to recite a *Markush* group thereby overcoming the rejection.

Accordingly, Applicants submit that Claims 10, 14, 18-21, 31, 33-42, 52 and 54-64 now satisfy the requirements of Section 112, second paragraph, and request that the rejections be withdrawn.

Rejections Under 5 U.S.C. § 102

Claims 1, 6, 8, 9-21, 22, 27, 29-43, 48, 50-66 and 108 stand rejected under 35 U.S.C. 102(e) as being anticipated by Pati *et al.* Applicants have canceled claims 6, 27, and 48 thereby rendering the rejections of these claims moot. Applicants respectfully traverse the rejections as to the remaining claims.

As the Examiner is aware, to anticipate a claim under 102 (e), the reference must teach every element of the claim (M.P.E.P.§ 2131).

1. The Invention

The present invention teaches compositions comprising two single-stranded targeting polynucleotides, each having a locking sequence and homology clamps, and a recombinase. The homology clamps are substantially homologous to a target nucleic acid. The locking sequences are capable of forming a secondary structure. The recombinase, in combination with the homology clamps drive the formation of D-Loops between the probes and the target sequence. The locking sequences form non-Watson-Crick complexes such as triplexes, Z-DNA anchors or quadruplexes that prevent DNA rotation, thereby stabilizing the double D-Loop complex.

The present invention also teaches additional examples of locks for D-loop stability e.g.; locks formed by the stacking of intercalating agents between bases of the probe strands,

or locks formed when an additional third probe (referred to as the secondary probe) which has complementary regions to specific portions in each probe are and thereby locks the D-loop (see specification: fig. 2E). Together, these locks prevent DNA rotation and make the D-loop thermally stable up to 65°C (see specification, p.38, Example 1, lines 38-40 and p.42, line 35 through p.43, line 1) in addition to stabilizing them to deproteinization. When tested by Applicants, Pati's structures were thermally less stable in comparison to the locked hybrids (see current Specification: p 42, line 37-39). Hence, the D-loop compositions taught in this application are novel and superior over the prior art.

2. The Rejection Over Pati *et al.*

Claim 1 recites, *inter alia* , two single-stranded targeting polynucleotide each having (i) at least one homology clamp that substantially corresponds to a preselected target sequence and (ii) at least one locking sequence. In practice, the locking sequence forms a lock structure to stabilize a double D-Loop structure formed by the single-stranded targeting polynucleotides and said target nucleic acid.

The Examiner argues that Pati *et al.* teach an anchoring sequence as recited in the Claim 1 prior to the present amendment. Applicants respectfully disagree. Nevertheless, the Applicants have amended Claim 1 to more distinctly claim that which is considered to be the invention.

Pati *et al.* teach a composition that forms stabilized double D-loops between two substantially complementary single-stranded targeting probes and a target sequence. The stabilization results from Watson-Crick base pairing between internal homology clamps on the two substantially complementary single-stranded probes. More specifically, the substantially complementary single-stranded targeting probes have external homology clamps flanking an internal homology clamp. *See, e.g.,* Col. 19, line 61- Col. 20, line 3; Col. 22, lines 31-59, and FIGS. 10, 13B and 13C. The internal homology clamps of the two substantially complementary single-stranded targeting probes are complementary to each other. Thus, the internal homology clamps of Pati *et al.* form Watson-Crick base pairs within the double D-Loop, thereby stabilizing the same. Col. 22, lines 31-59. It is noted that Pati *et al.* mention "heterologous inserts in the cssDNA probe". Col. 22, line 41. However, this is in reference to the internal homology clamps being heterologous with respect to the target, not with each

other. *Id.* Thus, Pati *et al.* teach that probes are substantially complementary to each other, that the internal homology clamps must be substantially complementary to themselves, and that the stabilization of the double D-Loop results from Watson-Crick base pairing between the complementary internal homology clamps.

Nowhere, however, do Pati *et al.* teach or suggest first and second single-stranded targeting polynucleotides each having, *inter alia*, locking sequences wherein said locking sequences form secondary, *i.e.*, non-Watson Crick, structure which stabilize the double D-Loop. Rather, and in distinct contrast, Pati *et al.* teach two substantially complementary probes each with an internal homology clamp that are substantially complementary to each other, *i.e.*, for Watson-Crick base pairing.

Independent Claims 1, 22, 43 and 108 recite locking sequences and thus are not anticipated by Pati *et al.*

The claims dependent on Claims 1, 22, 43 and 108 are also not anticipated bu Pati *et al.* since such claims are narrower in scope. The claims are therefore novel over Pati *et al.*

3. The Rejection Over Sena *et al.*

Claims 1, 6, 7, 12-14, 18-22, 27, 30, 33-35, 39-42 stand rejected under 35 U.S.C. §102(b) as being anticipated by Sena *et al.* Applicants have canceled claims 6, 27, 48, thereby rendering the rejections of these claims moot. Applicants respectfully traverse the rejections as to the remaining claims.

The recitations of Claims 1 and 22 are discussed above, and will not be further discussed here.

Sena *et al.* teach a composition that forms double D-loops between two complementary single-stranded targeting probes and a target sequence. Sena *et al.* does not teach heterology between the probes or between the probes and the target sequence.

Nowhere do Sena *et al.* teach or suggest single-stranded targeting polynucleotides each having, *inter alia*, a locking sequence, wherein said locking sequences form a secondary structure which stabilizes the double D-Loop. Rather, and in distinct contrast to Claim 1, Sena *et al.* teach two complementary probes, both of which are complementary to the target sequence.

Thus, Sena *et al.* fails to teach or suggest each and every element of Claims 1 and 22. Moreover, Claims 7, 12-14, 18-21, 30, 33-35, and 39-42 depend from either Claim 1 or Claim 22, and thus, Sena *et al.* fails to teach or suggest each and every element of these claims as well.

5. Conclusion

Accordingly, Applicants submit that Pati *et al.* do not teach or suggest each and every claim limitation recited in Claims 1, 8-22, 29-43, 50-66 and 108. Additionally Applicants respectfully submit that Sena *et al.* do not teach or suggest each and every claim limitation recited in Claims 1, 7, 12-14, 18-22, 30, 33-35, and 39-42 Accordingly, Applicants respectfully request the Examiner to withdraw the rejection of these claims under 35 U.S.C.§§ 102(e) and (b) respectively.

Rejections Under 35 U.S.C. § 103(a)

1. Legal Standard of Obviousness

As the Examiner is aware, to establish a *prima facie* case, three basic criteria must be met:(1) the prior art must provide one of ordinary skill with a suggestion or motivation to modify or combine the teachings of the references relied upon by the Examiner to arrive at the claimed invention; (2) the prior art must provide one of ordinary skill with a reasonable expectation of success; and (3) the prior art, either alone or in combination, must teach or suggest each and every limitation of the rejected claims. See M.P.E.P. § 2142.

The Federal Circuit has repeatedly warned that the requisite motivation to combine or modify references must come from the prior art, not the applicant's specification. *See, e.g., In re Dow Chem. Co.*, 5 USPQ2d 1529, 1531-32 (Fed. Cir. 1988). The mere fact that references can be modified does not render the resultant modification obvious unless the prior art also provides the motivation to combine or modify the references to arrive at the claimed invention. *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990); MPEP § 2143.01.

2. Claim 112

Claim 112 stands rejected under 35 U.S.C. §103(a) as being obvious over Pati *et al.* Pati *et al.* has been discussed above.

Claim 112 is the same as Claim 22 with the added limitation that a protein is bound to the lock structure. As discussed above, Pati *et al.* fail to teach or suggest every limitation of Claim 22. For this reason alone, the Examiner has failed to establish a *prima facie* case of obviousness against Claim 112. Accordingly, Applicants respectfully request the Examiner to withdraw the Rejection of Claim 112 under 35 U.S.C. §103(a).

3. Claims 1-3, 6, 8, 9-21, 22-24, 27, 29-42, 43-45, 48, 50-66 and 108

Claims 1-3, 6, 8, 9-21, 22-24, 27, 29-42, 43-45, 48, 50-66 and 108 stand rejected under 35 U.S.C. §103 (a) as being unpatentable over Pati *et al* as applied to claims 1, 6, 8, 9-21, 22, 27, 29-42, 43, 48, 50-66 and 108 and further in view of Helene *et al.*

Claims 6, 27 and 48 have been canceled thereby rendering rejections to these claims moot. Applicants traverse the rejections as to the rest of the claims on the ground that the Examiner has failed to establish a *prima facie* case of obviousness.

As discussed above, Pati *et al.* fails to teach or suggest each and every limitation of the claimed invention. In particular Pati *et al.* does not teach or suggest locking sequences that form secondary structures which stabilize the double D-Loop. Claims 1, 22, 108, 112 and the claims depending therefrom all call for a "locking sequence."

Helene *et al.* do not make up for the deficiencies in Pati *et al.* Helene *et al.* is a review article regarding the regulation of gene expression by antisense. In one aspect of the review the authors discuss probes that form triplex structures. However, nowhere does Helene *et al.* discuss, let alone teach or suggest, using recombinase mediated formation of stabled double D-Loop structures. Nowhere does Helen *et al.* discus, let alone suggest, a composition of two probes with locking sequences that result in double D-Loop stabilization by formation of a lock having secondary structure. Helene does not provide this suggestion alone or in combination with Pati *et al.*

Therefore, for this reason alone, the Examiner has failed to establish a *prima facie* case of obviousness against independent Claims 1, 22, 43, and 108, and against Claims 2, 3, 8, 9-24, 29-42, 44, 45, and 50-66 which depend from one of these independent claims.

Accordingly, Applicants submit that Claims 1-3, 6, 8, 9-21, 22-24, 27, 29-42, 43-45, 48, 50-66 and 108 are not obvious over Pati *et al.* in view of Helene *et al.* Accordingly Applicants respectfully request the Examiner to withdraw the rejection of these claims under 35 U.S.C. §103(a).

4. Claims 1, 5-8, 9-21, 22, 26-42, 43, 47-66 and 108

Claims 1, 5-8, 9-21, 22, 26-42, 43, 47-66 and 108 stand rejected under 35 U.S.C. §103 (a) as being unpatentable over Pati *et al.* as applied to claims 1, 6, 8, 9-21, 22, 27, 29-42, 43, 48, 50-66 and 108 and further in view of Barton. Claims 6, 27 and 48 have been canceled, thereby rendering rejections of these claims moot. Applicants traverse the rejections as to the rest of the claims on the ground that the Examiner has failed to establish a *prima facie* conclusion of obviousness.

As discussed above, Pati *et al.* fails to teach or suggest each and every limitation of the claimed invention. In particular Pati *et al.* does not teach or suggest locking sequence as recited in Claims 1, 22, 43, 108, 112 and the claims depending therefrom.

Barton does not make up for the deficiencies in Pati *et al.* Barton teaches compositions for labeling and cleaving Z- and A- DNA using substituted 1,10-phenanthroline. Barton does not teach double D-loops structures and improved thermal stability of D-loops. Nowhere does Barton discuss , let alone teach or suggest, using recombinase mediated formation of stable double D-Loop structures. Nowhere does Barton discuss a composition of two probes with "locking sequence" or the resulting double D-Loops stabilized by the lock structure formed by the locking sequence.

Therefore, for this reason alone, the Examiner has failed to establish a *prima facie* case of obviousness against independent Claims 1, 22, 43, and 108, and against Claims 5-21, 26-42, and 47-66 which depend from one of these independent claims.

Accordingly, Applicants submit that Claims 1, 5-22, 26-43, 47-66 and 108 are not obvious over Pati *et al.* in view of Barton. Accordingly Applicants respectfully request the Examiner to withdraw the rejection of these claims under 35 U.S.C. §103(a).

5. Claims 1, 4, 6, 8, 9-21, 22, 25, 27, 29-42, 43, 46, 48, 50-66 and 108

Claims 1, 4, 6, 8, 9-21, 22, 25, 27, 29-42, 43, 46, 48, 50-66 and 108 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Pati *et al.* as applied to claims 1, 6, 8, 9-21, 22, 27, 29-42, 43, 48, 50-66 and 108 and further in view of Simonsson *et al.* Claims 6, 27 and 48 have been canceled, thereby rendering rejections of these claims moot. Applicants traverse the rejections as to the rest of the claims on the ground that the Examiner has failed to establish a *prima facie* conclusion of obviousness.

As discussed above, Pati *et al.* fails to teach or suggest each and every limitation of the claimed invention. In particular Pati *et al.* does not teach or suggest locking sequences as recited in Claims 1, 22, 43, 108, 112 and the claims depending therefrom.

Simonsson *et al.* does not make up for the deficiencies in Pati *et al.* Simonsson *et al.* Simonsson *et al.* teach a tetraplex that is important in the activation of c-myc transcription. Simonsson *et al.* does not teach D-loops or use of the tetraplex in stabilization of D-loops. Nowhere do Simonsson *et al.* discuss, let alone teach or suggest, using recombinase mediated formation of stable double D-Loop structures. Nowhere do Simonsson *et al.* discuss, let alone teach or suggest, a composition of two probes with locking sequences or the resulting double D-Loops stabilized by a lock structure formed by the locking sequence.

Therefore, for this reason alone, the Examiner has failed to establish a *prima facie* conclusion of obviousness against independent Claims 1, 22, 43, and 108, and against Claims 8-21, 29-42, 43 and 50-66 which depend from one of these independent claims. Thus, for this reason alone the Examiner has failed to establish a *prima facie case* against the claimed invention.

Accordingly, Applicants respectfully submit that claims 1, 4, 8, 9-21, 22, 25, 29-42, 43, 46, 50-66 and 108 are not obvious over Pati *et al.* in view Simonsson *et al.* and request that the §103 (a) rejections be withdrawn.

Conclusion

Applicants submit that all the claims are in condition for allowance and an early notification of such is solicited.

The Commissioner is hereby authorized to charge any additional fees, including extension fees, to Deposit Account No. 06-1300 (Order No. A-68112-1/RFT/BTC/DLR).

Respectfully submitted,

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APPENDIX
"Version with markings to show changes made"

IN THE SPECIFICATION:

Paragraph beginning at page 4, line 27, has been amended as follows:

--Figures 2A-F depict examples of double D-loop structures. Blank squares depict non-Watson-Crick base pairing. Filled in squares depict Watson-Crick base pairing. Figure 2A depicts a double D-loop without an internal anchoring sequence. Figure 2B depicts a duplex forming heterologous insert through Watson-Crick base pairing. Figure 2C depicts a triplex-forming heterologous insert which is also a locking sequence that prevents DNA rotation. Figure 2D depicts a quadruplex forming heterologous insert which is also a locking sequence that prevents DNA rotation. Figure 2E depicts a heterologous insert which forms a triplex with a secondary probe, thereby forming a locking sequence that prevents DNA rotation. Figure 2F depicts a double D-loop in which the internal homology clamp or anchoring sequence is formed from the target sequences, i.e. wherein the targeting polynucleotides are shorter than the target sequence. --

Paragraph beginning at page 6, line 1, has been amended as follows:

– Figure 9C depicts DNA probe oligonucleotides QI_W (SEQ ID NO:5) and QI_C (SEQ ID NO:6) (Quadruple DNA-forming insert) contains the heterologous insert sequence$T_2G_4T_2G_4T_2$. ~~(SEQ ID NO:12)~~ (SEQ ID NO:9) "b": biotin. –

Paragraph beginning at page 11, line 4, has been amended as follows:

– The crystal structure of RecA protein in the absence of DNA reveals two disordered polypeptide loops, L1 and L2, that are proposed nucleic acid binding sites (Story et al, Nature 355(6358):318-325 (1992)). Several lines of evidence indicate that loop L2 is the oligonucleotide binding domain: a) proteolysis of ssDNA-RecA complexes yields a unique 4-kD peptide protected by the DNA that spans this loop (Gardner et al., Eur J. Biochem. 233:419-425 (1995)); b) crosslinks between a ssDNA and RecA map to loops L1 and L2; c) the intrinsic fluoresescence of peptides in loop2 is quenched in RecA-DNA complexes; and d) the 20 amino acid FECO peptide corresponding to the L2 polypeptide loop (NQIRMKIGVMFGNPETTTGG) ~~(SEQ ID NO:13)~~ (SEQ ID NO:12) binds to ssDNA. –

Paragraph beginning at page 12, line 1, has been amended as follows:

– Accordingly, in one embodiment, FECO oligopeptide (NQIRMKIGVMFGNPETTTGG) ~~(SEQ ID NO:14)~~ (SEQ ID NO:12) and NLS-FECO (PLLLALVNQIRMKIGVMFGNPETTTGG) ~~(SEQ ID NO:14)~~ (SEQ ID NO:13) are used to for specific gene targeting and by locked D-loop hybrids. E. coli

RecA protein does not contain a eukaryotic cell nuclear localization signal (NLS) facilitating the transport of exogenously added proteins to the nucleus. Certain oligopeptides and proteins that do not have the NLS signal are not actively transported into the nucleus. For example, it has been shown by immunofluorescence staining that when wild type RecA protein is microinjected into the cytoplasm of certain human cells, it remains in the cytoplasm and it does not significantly enter the nucleus (Kido et al., Exp. Cell Res. 198:107-114 (1992)). In eukaryotic cells, nuclear proteins are initially synthesized in the cytoplasm and then are rapidly transported into the nucleus. The precise mechanism of nuclear transport is not fully known, and active transport has been suggested (Yamaizumi et al., Nature 273:782-784 (1978); Sugawa et al., Exp. cell Res. 159:419-429 (1985)); Tsuneoka et al., J. Biol. Chem. 261:1829-1834 (1986); Imamoto-Sonobe et al., Proc. Natl. Acad. Sci. USA 85:3426-3430 (1988)). Kalderon et al., Nature 311:5981 (1984a); Kalderon et al. Cell 3:499-509 (1984b)). Kalderon et al., (1984a, b), showed that a short oligopeptide sequence of the SV40 virus large T-antigen, PLLLALV ~~(SEQ ID NO:15)~~ (SEQ ID NO:14), specifies a nuclear localization signal (NLS) (Kalderon et al., 1984a and 1984b). Fusion of exogenous proteins with this viral NLS peptide has also been shown to direct the transport of fused exogenous proteins into the nucleus. For example, when this viral NLS peptide was fused to the RecA protein and injected into the cytoplasm, the PLLLALV (SEQ ID NO:14) modified RecA protein was efficiently transported to the nucleus (Kido et al., 1992). More importantly, the NLS fused RecA protein retains its full in vivo RecA activity. –

Paragraph beginning at page 12, line 37, has been amended as follows:

– In a preferred embodiment, the 20 amino acid FECO peptide (NQIRMKIGVMFGNPETTTGG) (SEQ ID NO:12) and FECO with a NLS (PLLLALVNQIRMKIGVMFGNPETTTGG) (SEQ ID NO:13) attached to the N-terminal end are used for cssDNA targeting to a homology clamped site in the duplex DNA. –

Paragraph beginning at page 14, line 28, has been amended as follows:

– Targeting polynucleotides have a number of relevant structures. In a preferred embodiment, the target polynucleotides comprise homology clamps, i.e. sequences that substantially correspond to, or are substantially complementary to, a predetermined endogenous DNA sequence. The term "corresponds to" is used herein to mean that a polynucleotide sequence is homologous (i.e., may be similar or identical, not strictly evolutionarily related) to all or a portion of a reference polynucleotide sequence, or that a polynucleotide sequence is identical to a reference polynucleotide sequence. In contradistinction, the term "complementary to" is used herein to mean that the complementary sequence is homologous to all or a portion of a reference polynucleotide sequence. As outlined below, preferably, the homology is at least 70%, preferably 85%, and more preferably 95% identical. Thus, the complementarity between two single-stranded targeting polynucleotides need not be perfect. For illustration, the nucleotide sequence "TATAC" (SEQ ID NO:15) corresponds to or is

identical to a reference sequence "TATAC" (SEQ ID NO:15) and is perfectly complementary to a reference sequence "GTATA" (SEQ ID NO:16). –

Paragraph beginning at page 38, line 25, has been amended as follows:

– Three sets of complementary single stranded (css) probes were designed as follows. The target sequence was the 62 nucleotides from bases 667 to 723 of pBluescript II SK(−) (Stratagene. LaJolla, CA; Figure 9A). The control reaction comprises two complementary single stranded nucleic acids (cssDNA) comprising these 62 bases and their complement. Targeting polynucleotides comprising the quadruplex forming lock 5-TTGGGGTTGGGGTT ~~(SEQ ID NO:16)~~ (SEQ ID NO:9) are shown in Figure 9C (Sundquist et al., (1989)). Targeting polynucleotides also were made comprising the triplex forming lock GGGTGGTGGGTGGGGTATTAGGGGAGGGAGGAGGG (SEQ ID NO:17) inserted in the sequence (Dayn et al., PNAS USA 89:11406 (1992)). –

Paragraph beginning at page 45, line 16, has been amended as follows:

– In these experiments a modified version of *in vitro* transcription assay described by Golub *et al.*, (1992, 1993, *supra*) was used. Briefly, double-stranded DNA fragments having about 300 bp of homology (including T7 promoter) with pBluescript II SK(-) were obtained by PCR either from pBluescript II SK(-) or pTL plasmid (pTL plasmid was derived from pBluescript II SK(-) by inserting the triplex forming sequence, 5-GGGTGGTGGGTGGGGTATTAGGGGAGGGGAGGAGG-3 (SEQ ID NO:17) (Dayn *et al.*, 1992, *supra*) into the *Hin*dIII/*Eco*RI site; Figure 16). The probes obtained from pTL plasmid were designed to form a triplex lock when targeted to pBluescript II SK(-). In addition, probes shown in Figure 9A-C (SEQ ID NO:1-6) also are used. –

On page 70, immediately preceding the claims, the enclosed Sequence Listing was added to the text:

IN THE CLAIMS:

1. (Amended) A composition comprising at least one recombinase and two substantially complementary single stranded targeting polynucleotides, each ~~containing~~ comprising:

a) at least one homology clamp that substantially corresponds to or is substantially complementary to a preselected target nucleic acid sequence; and

b) at least one locking ~~anchoring~~ sequence.

2. (Amended) The composition of claim 1 further comprising a secondary probe, wherein said probe is substantially complementary to at least one of said ~~anchoring~~ locking sequences.

3. (Amended) The composition of claim 1 wherein said ~~anchoring~~ locking sequences form a triplex anchor.

4. (Amended) The composition of claim 1 wherein said locking ~~anchoring~~ sequences form a quadruplex anchor.

5. (Amended) The composition of claim 1 wherein said locking ~~anchoring~~ sequences form a Z-DNA anchor.

7. (Amended) The composition of claim 1 wherein said locking ~~anchoring~~ sequences form an A-DNA anchor.

8. (Amended) The composition of claim 1 wherein said locking ~~anchoring~~ sequences comprise RNA.

9. (Amended) The composition of claim 1 wherein said locking ~~anchoring~~ sequences comprise DNA.

10. (Amended) The composition of claim 1 wherein at one of said targeting polynucleotides comprises ~~protein~~ a peptide nucleic acid.

11. (Amended) The composition of claim 1 wherein said locking ~~anchoring~~ sequences comprise DNA and RNA.

14. (Amended) The composition of Claim 13 ~~12~~, wherein said RecA protein species is *E. coli* RecA.

21. (Amended) The composition of claim 18 wherein said substituent is selected from the group consisting of intercalators, cross-linking moieties, labels, photoactive moieties, nucleic acid scission inducing moieties, purification tag moieties, and nucleic acid modification moieties.

22. (Amended) A composition comprising at least one recombinase and a double D-loop comprising a target nucleic acid and two substantially complementary single stranded targeting polynucleotides, each comprising ~~containing~~:

a) at least one homology clamp that substantially corresponds to or is substantially complementary to a preselected target nucleic acid ~~sequence of said target nucleic acid~~ and to each other; and

b) at least one locking ~~anchoring~~ sequence.

23. (Amended) The composition of claim 22 further comprising a secondary probe, wherein said probe is substantially complementary to at least one of said locking ~~anchoring~~ sequences.

24. (Amended) The composition of claim 22 wherein said locking ~~anchoring~~ sequences form a triplex anchor.

25. (Amended) The composition of claim 22 wherein said locking ~~anchoring~~ sequences form a quadruplex anchor.

26. (Amended) The composition of claim 22 wherein said locking ~~anchoring~~ sequences form a Z-DNA anchor.

28. (Amended) The composition of claim 22 wherein said locking ~~anchoring~~ sequences form an A-DNA anchor.

29. (Amended) The composition of claim 22 wherein said locking ~~anchoring~~ sequences comprise RNA.

30. (Amended) The composition of claim 22 wherein said locking ~~anchoring~~ sequences comprise DNA.

31. (Amended) The composition of claim 22 wherein at least one of said targeting polynucleotides comprises ~~protein~~ a peptide nucleic acid.

32. (Amended) The composition of claim 22 wherein said locking ~~anchoring~~ sequences comprise DNA and RNA.

35. (Amended) The composition of Claim 34 ~~33~~, wherein said prokaryotic RecA protein ~~species~~ is *E. coli* RecA.

39. (Amended) The composition of claim 22 wherein at least one of said single stranded nucleic acids comprises ~~contains~~ at least one substituent.

42. (Amended) The composition of claim 40 wherein said substituent is selected from the group consisting of intercalators, cross-linking moieties, labels, photoactive moieties, nucleic acid scission inducing moieties, purification tag moieties, and nucleic acid modification moieties.

43. (Amended) A composition comprising at least one recombinase and a double D-loop comprising a target nucleic acid and a single stranded targeting polynucleotides comprising a first homology clamp that substantially corresponds to a preselected target nucleic acid sequence, a second homology clamp that is substantially complementary to said preselected target nucleic acid sequence, and at least one locking ~~anchoring~~ sequence.

44. (Amended) The composition of claim 43 further comprising a secondary probe, wherein said probe is substantially complementary to at least one of forms a lock structure with said locking ~~anchoring~~ sequences.

45. (Amended) The composition of claim 43 wherein said locking ~~anchoring~~ sequences form a triplex anchor.

46. (Amended) The composition of claim 43 wherein said locking ~~anchoring~~ sequences form a quadruplex anchor.

47. (Amended) The composition of claim 43 wherein said locking ~~anchoring~~ sequences form a Z-DNA anchor.

49. (Amended) The composition of claim 43 wherein said locking ~~anchoring~~ sequences form an A-DNA anchor.

50. (Amended) The composition of claim 43 wherein said locking ~~anchoring~~ sequences comprise RNA.

51. (Amended) The composition of claim 43 wherein said locking ~~anchoring~~ sequences comprise DNA.

52. (Amended) The composition of claim 43 wherein at least one of said targeting polynucleotides comprises ~~protein~~ a peptide nucleic acid.

53. (Amended) The composition of claim 43 wherein said locking ~~anchoring~~ sequences comprise DNA and RNA.

60. (Amended) The composition of claim 43 wherein at least one of said single stranded nucleic acids comprises ~~contains~~ at least one substituent.

63. (Amended) The composition of claim 60 wherein said substituent is selected from the group consisting of intercalators, cross-linking moieties, labels, photoactive moieties, nucleic acid scission inducing moieties, purification tag moieties, and nucleic acid modification moieties.

64. (Amended) A cell comprising a ~~containing the~~ composition selected from ~~of~~ claims 1, 20, or 43.

108. (Amended) A kit comprising at least one recombinase and two substantially complementary single stranded targeting polynucleotides, each comprising ~~containing~~:

a) at least one homology clamp that substantially corresponds to or is substantially complementary to a preselected target nucleic acid sequence; and
b) at least one locking ~~anchoring~~ sequence.

112. (Amended) A composition comprising a double D-loop comprising a target nucleic acid and two substantially complementary single stranded targeting polynucleotides, each comprising ~~containing~~:

i) at least one homology clamp that substantially corresponds to or is substantially complementary to a preselected target nucleic acid sequence of said target nucleic acid and to each other;

ii) at least one locking ~~anchoring~~ sequence; wherein said locking ~~anchoring~~ sequence forms a lock ~~an anchoring structure~~ and a protein ~~bound~~ binds to said lock ~~anchoring structure~~.

Appendix of Pending Claims
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1. A composition comprising at least one recombinase and two substantially complementary single stranded targeting polynucleotides, each comprising:
   a) at least one homology clamp that substantially corresponds to or is substantially complementary to a preselected target nucleic acid sequence; and
   b) at least one locking sequence.

2. The composition of claim 1 further comprising a secondary probe, wherein said probe is substantially complementary to at least one of said locking sequences.

3. The composition of claim 1 wherein said locking sequences form a triplex anchor.

4. The composition of claim 1 wherein said locking sequences form a quadruplex anchor.

5. The composition of claim 1 wherein said locking sequences form a Z-DNA anchor.

7. The composition of claim 1 wherein said locking sequences form an A-DNA anchor.

8. The composition of claim 1 wherein said locking sequences comprise RNA.

9. The composition of claim 1 wherein said locking sequences comprise DNA.

10. The composition of claim 1 wherein at one of said targeting polynucleotides comprises a peptide nucleic acid.

11. The composition of claim 1 wherein said locking sequences comprise DNA and RNA.

12. The composition of claim 1, wherein said recombinase is a species of prokaryotic recombinase.

13 The composition of Claim 12, wherein said prokaryotic recombinase is a species of prokaryotic RecA protein.

14. The composition of Claim 13 wherein said RecA protein species is *E. coli* RecA.

15. The composition of claim 1, wherein said recombinase is a species of eukaryotic recombinase.

16. The composition of claim 15, wherein said recombinase is a Rad51 recombinase.

17. The composition of claim 15, wherein said eukaryotic recombinase is a complex of recombinase proteins.

18. The composition of claim 1 wherein at least one of said single stranded nucleic acids contains at least one substituent.

19. The composition of claim 18 wherein said substituent is a chemical substituent.

20. The composition of claim 18 wherein said substituent is a protein.

21. The composition of claim 18 wherein said substituent is selected from the group consisting of intercalators, cross-linking moieties, labels, photoactive moieties, nucleic acid scission inducing moieties, purification tag moieties, and nucleic acid modification moieties.

22. A composition comprising at least one recombinase and a double D-loop comprising a target nucleic acid and two substantially complementary single stranded targeting polynucleotides, each comprising:

a) at least one homology clamp that substantially corresponds to or is substantially complementary to a preselected target nucleic acid and to each other; and

b) at least one locking sequence.

23. The composition of claim 22 further comprising a secondary probe, wherein said probe is substantially complementary to at least one of said locking sequences.

24. The composition of claim 22 wherein said locking sequences form a triplex anchor.

25. The composition of claim 22 wherein said locking sequences form a quadruplex anchor.

26. The composition of claim 22 wherein said locking sequences form a Z-DNA anchor.

28. The composition of claim 22 wherein said locking sequences form an A-DNA anchor.

29. The composition of claim 22 wherein said locking sequences comprise RNA.

30. The composition of claim 22 wherein said locking sequences comprise DNA.

31. The composition of claim 22 wherein at least one of said targeting polynucleotides comprises a peptide nucleic acid.

32. The composition of claim 22 wherein said locking sequences comprise DNA and RNA.

33. The composition of claim 22, wherein said recombinase is a species of prokaryotic recombinase.

34. The composition of Claim 33, wherein said prokaryotic recombinase is a species of prokaryotic RecA protein.

35. The composition of Claim 34, wherein said prokaryotic RecA protein is *E. coli* RecA.

36. The composition of claim 22, wherein said recombinase is a species of eukaryotic recombinase.

37. The composition of claim 36, wherein said recombinase is a Rad51 recombinase.

38. The composition of claim 36, wherein said eukaryotic recombinase is a complex of recombinase proteins.

39. The composition of claim 22 wherein at least one of said single stranded nucleic acids comprises at least one substituent.

40. The composition of claim 39 wherein said substituent is a chemical substituent.

41. The composition of claim 39 wherein said substituent is a protein.

42. The composition of claim 40 wherein said substituent is selected from the group consisting of intercalators, cross-linking moieties, labels, photoactive moieties, nucleic acid scission inducing moieties, purification tag moieties, and nucleic acid modification moieties.

43. A composition comprising at least one recombinase and a double D-loop comprising a target nucleic acid and a single stranded targeting polynucleotides comprising a first homology clamp that substantially corresponds to a preselected target nucleic acid sequence, a second homology clamp that is substantially complementary to said preselected target nucleic acid sequence, and at least one locking sequence.

44. The composition of claim 43 further comprising a secondary probe, wherein said probe is substantially complementary to at least one of forms a lock structure with said locking sequences.

45. The composition of claim 43 wherein said locking sequences form a triplex anchor.

46. The composition of claim 43 wherein said locking sequences form a quadruplex anchor.

47. The composition of claim 43 wherein said locking sequences form a Z-DNA anchor.

49. The composition of claim 43 wherein said locking sequences form an A-DNA anchor.

50. The composition of claim 43 wherein said locking sequences comprise RNA.

51. The composition of claim 43 wherein said locking sequences comprise DNA.

52. The composition of claim 43 wherein at least one of said targeting polynucleotides comprises a peptide nucleic acid.

53. The composition of claim 43 wherein said locking sequences comprise DNA and RNA.

54. The composition of claim 43, wherein said recombinase is a species of prokaryotic recombinase.

55. The composition of Claim 54, wherein said prokaryotic recombinase is a species of prokaryotic RecA protein.

56. The composition of Claim 55, wherein said RecA protein species is *E. coli* RecA.

57. The composition of claim 43, wherein said recombinase is a species of eukaryotic recombinase.

58. The composition of claim 57, wherein said recombinase is a Rad51 recombinase.

59. The composition of claim 57, wherein said eukaryotic recombinase is a complex of recombinase proteins.

60. The composition of claim 43 wherein at least one of said single stranded nucleic acids comprises at least one substituent.

61. The composition of claim 60 wherein said substituent is a chemical substituent.

62. The composition of claim 60 wherein said substituent is a protein.

63. The composition of claim 60 wherein said substituent is selected from the group consisting of intercalators, cross-linking moieties, labels, photoactive moieties, nucleic acid scission inducing moieties, purification tag moieties, and nucleic acid modification moieties.

64. A cell comprising a composition selected from claims 1, 20, or 43.

65. The cell of claim 64 which is a eukaryotic cell.

66. The cell of claim 64 which is a prokaryotic cell.

108. A kit comprising at least one recombinase and two substantially complementary single stranded targeting polynucleotides, each comprising

a) at least one homology clamp that substantially corresponds to or is substantially complementary to a preselected target nucleic acid sequence; and
b) at least one locking sequence.

112. A composition comprising a double D-loop comprising a target nucleic acid and two substantially complementary single stranded targeting polynucleotides, each comprising.

i) at least one homology clamp that substantially corresponds to or is substantially complementary to a preselected target nucleic acid sequence of said target nucleic acid and to each other;

ii) at least one locking sequence; wherein said locking sequence forms a lock and a protein binds to said lock.